Emergency Planning and the Acute Toxic Potency of Inhaled Ammonia

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Ammonia is present in agriculture and commerce in many if not most communities. This report evaluates the toxic potency of ammonia, based on three types of data: anecdotal data, in some cases predating World War I, reconstructions of contemporary industrial accidents, and animal bioassays. Standards and guidelines for human exposure have been driven largely by the anecdotal data, suggesting that ammonia at 5,000–10,000 parts per million, volume/volume (ppm-v), might be lethal within 5–10 min. However, contemporary accident reconstructions suggest that ammonia lethality requires higher concentrations. For example, 33,737 ppm-v was a 5-min zero-mortality value in a major ammonia release in 1973 in South Africa. Comparisons of secondary reports of ammonia lethality with original sources revealed discrepancies in contemporary sources, apparently resulting from failure to examine old documents or accurately translate foreign documents. The present investigation revealed that contemporary accident reconstructions yield ammonia lethality levels comparable to those in dozens of reports of animal bioassays, after adjustment of concentrations to human equivalent concentrations via U.S. Environmental Protection Agency (EPA) procedures. Ammonia levels potentially causing irreversible injury or impairing the ability of exposed people to escape from further exposure or from coincident perils similarly have been biased downwardly in contemporary sources. The EPA has identified ammonia as one of 366 extremely hazardous substances subject to community right-to-know provisions of the Superfund Act and emergency planning provisions of the Clean Air Act. The Clean Air Act defines emergency planning zones (EPZs) around industrial facilities exceeding a threshold quantity of ammonia on-site. This study suggests that EPZ areas around ammonia facilities can be reduced, thereby also reducing emergency planning costs, which will vary roughly with the EPZ radius squared. *Key words*: air pollutant, ammonia, emergency planning, health risk assessment, human health, inhalation, respiratory irritant. *Environ Health Perspect* 107:617–627 (1999). [Online 23 June 1999]
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In 1984 methyl isocyanate was released from a chemical plant in Bhopal, India. The release reportedly killed thousands of residents and irreversibly injured the eyes and lungs of approximately 20,000 (*1*). Internationally, governments recognized the need to identify extremely hazardous substances (EHSs) and assist communities in preparing for chemical emergencies. The U.S. Environmental Protection Agency (EPA) identified 366 EHSs, as required by the Community Right-To-Know Act (*2*). Community emergency planning requirements followed under the Risk Management Program (RMP) in Section 112(r) of the 1990 Clean Air Act Amendments (*3*).

Industrial facilities exceeding threshold quantities of EHSs on site are subject to the RMP. The RMP defines emergency planning zones (EPZs) around facilities, and requires facilities to submit to the EPA a risk management plan aimed at preventing catastrophic chemical releases and averting Bhopal-type consequences of releases. The cost of community emergency planning for a facility is likely to roughly depend on the area of its EPZ, which in turn depends on the square of the radius around the facility deemed necessary to attenuate a worst-case chemical release to specified airborne concentrations, termed acute exposure guideline levels (AEGLs).

The AEGLs for each EHS have nothing to do with routinely acceptable exposures. Acceptable community and occupational levels are set by a host of more conservative parameters. Rather, the AEGLs must be established to protect members of the general population in the context of "exposure at high levels but of short duration, usually less than one hour, and only once in a lifetime" (*1*). The AEGLs are under development by the National Advisory Committee (NAC) on AEGLs. NAC AEGL composition is legislatively defined to assure balance, although NAC AEGL deliberations about ammonia began before the committee reached its full complement. Ammonia was one of the first EHSs to be addressed by NAC AEGL, and is of great concern both to companies and communities (*4*):

> During the 20th century, humanity has almost quadrupled its numbers. Although many factors have fostered this unprecedented expansion, its continuation during the past generation would not have been at all possible without a widespread—yet generally unappreciated—activity: the synthesis of ammonia.

Three types of AEGLs are defined by the National Research Council (*1*): AEGL-1, to protect against nuisance exposure; AEGL-2, to protect against irreversible injury or disability (including impairment of the ability to escape); and AEGL-3, to protect against lethality. Each type of AEGL is quantified via multiple combinations of airborne concentration and exposure duration (5 min, 30 min, 1 hr, 4 hr, and 8 hr) to protect against effects of concern in exposures lasting from minutes to hours.

This assessment of the acute toxicologic potency of ammonia critically evaluates available toxicologic and accident reconstruction data, updating air dispersion modeling results to quantify concentrations to which victims probably were exposed more accurately than older models could. This investigation assumes that gaseous anhydrous ammonia is released in the vicinity of employees wearing no protective breathing apparatus, or that unprotected members of the general public encounter it. Chemical risks posed by ammonium, ammonium salts, and liquid ammonia are excluded from consideration. Also, cryogenic, high-pressure, and high temperature risks are excluded.

Methods

Standard procedures of technical information acquisition were used. These included online and in-house database and literature searches and the acquisition of selected documents. Specific information about the Potchefstroom, South Africa, ammonia release was provided by ERM-Four Elements (Columbus, OH), and apparently represents the same information as that published by Lonsdale (*5*) and Pederson and

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Selig (*6*). Acceptance criteria for input data for the present assessment were adopted, and articles were examined to identify toxicologic information conforming with these criteria. To be accepted for quantitative analysis, studies must have identified the test species and reported acute toxic inhalation effect(s) and exposure regimens, including concentration(s) in air and duration(s) of exposure. Concentrations to which animals were exposed in bioassays were adjusted to human equivalent concentrations (HECs) using parameters for dose conversion among species (*7,8*) and standard EPA methodology for irritant gases (*8*).

Results

Odor and Odor Threshold

The odor of ammonia is distinct, pungent, and often familiar because of its common use in cleaning. Several reports of the odor threshold for airborne ammonia have been published. These include values of 25 parts per million, volume/volume (ppm-v) (*9,10*), 48 ppm-v (*10,11*), 46.8 ppm-v (*12,13*), and 0.0266–39.6 mg/m^3 (0.04–57 ppm-v) (*13,14*). The presence of airborne ammonia may become apparent to exposed individuals at concentrations in air roughly in the range of occupational exposure limits.

Vapor Density

The molecular weight of ammonia (NH_3) is 17.03 d (g/mol) (*10,15–17*). Its vapor density is 0.6 relative to air, which is assigned a reference vapor density of unity (= 1) (*13,17*). The density of liquid ammonia at one atmosphere pressure (and -33.35° C) is 0.6818 (*15*). The density of mixtures of ammonia with water (ammonia water) depends on the ammonia fraction. The density is 0.957 for a 10% ammonia solution and 0.90 for a Spirit of Hartshorn solution, which is 28–29% ammonia.

Acute Toxic Inhalation Effects

Reversible or clinically insignificant effects. Several reports of reversible or clinically insignificant effects exerted by ammonia on humans were located (Table 1). These effects include eye irritation (*10,13,18–20*), upper airway irritation (*10,13,18–20*), lacrimation (*10,13,18–20*), altered breathing patterns (*10,19*), minor biochemical changes (*13,21*), and minor blood pressure and pulse rate changes (*10,19*). Similar effects were also reported in animal studies. The lowest exposure concentration eliciting effects was 50 ppm-v over a duration of 10 min, causing faint to moderate irritation of the human upper airway (*13,18*).

Irreversible injury: animal studies. Several reports of potentially irreversible nonlethal clinical effects involving bioassay animals were located. Bioassay animals exhibiting such effects included mice (*10,12,25–27*), rats (*10,13,28*), rabbits (*10,13,18,22,27,29*), and cats (*13,18,27,29*).

Irreversible injury: human studies. Examination of Table 1 reveals no reports of potentially irreversible nonlethal clinical effects in humans. Accident reports reveal two accidents involving permanent injuries, including impaired breathing and damage to the respiratory system, throat, and eyes (*30*). However, the estimated ammonia concentration range is unhelpfully broad (700–10,000 ppm-v) and exposure durations are unstated.

Fatal exposure: animal studies. Studies of ammonia-induced mortality in animal bioassays are set forth in Table 2. A 1-hr median lethal concentration (LC_{50}) value for cats exposed to airborne ammonia was 1,071 ppm-v (*31,32*). Numerous bioassay reports are analyzed in Table 2, giving equivalent 5-, 30-, and 60-min human inhalation lowest lethal concentration (LC_{LO}) and LC_{50} values in accordance with the equation $C^n(t)$ = constant, using n = 1 (Haber's rule) and n = 2 (*33*).

Fatal exposure: human studies. Examination of Table 1 reveals several reports of human mortality following exposure to airborne ammonia at a concentration of 5,000 ppm-v. Concentrations are typically estimates obtained from accident reconstructions. One report indicates immediate death from spasm, inflammation, or edema of the larynx (*13,34*). Other reports indicate exposure durations of 5 min (*27,35,36*) or 30 min (*10,37*). A different lethality benchmark—7,000 ppm-v over 3 hr exposure—was reported in a draft Environment Canada document (*13,38*). Selected reports of human lethality were examined to distinguish between primary research or clinical reports versus secondary reviews. The evolution of reported lethality benchmark values is traced over time in Figure 1.

Environment Canada (*38*). The 1981 draft is out of print, superseded by a July 1984 final report. The 5,000-ppm-v lethality concentration remains. The Environment Canada (*38*) document source is the 1978 edition of the *Encyclopedia of Chemical Technology* (*39*), specifically a table referred to by Environment Canada (*38*) as a "Summary of Human Exposure." In the Kirk-Othmer table (*39*), 5,000 ppm-v (7,179 mg/m^3) is associated with "serious edema, strangulation, asphyxia; fatal almost immediately."

Environment Canada (*38*) also provides Table 7.4.1 "Inhalation," in which literature on effects and effect concentrations is cited. The Kirk-Othmer (*39*) citation and effect concentration are not used. However, ammonia is associated with (apparently lethal) "respiratory spasm and rapid asphyxia" in a range of 3,500–7,000 mg/m^3 (approximately 2,500–5,000 ppm-v) by Braker and Mossman (*40*). The same range is cited in a National Research Council report (*41*), which also indicates a 0.5- to 1-hr exposure duration. The Environment Canada table (*38*) cites a Registry of Toxic Effects of Chemical Substances (RTECS) report (*27*) of a 5-min LC_{LO} of 21,000 mg/m^3 (approximately 30,000 ppm-v). Table 7.4.1 also cites a 3-hr LC_{LO} of 7,000 µg/m^3 (approximately 10,000 ppm-v) reported by the International Technical Information Institute (ITII) (*42*).

The Environment Canada report (*38*) is a secondary source; the source quality is low. [See Kirk-Othmer (*39*), Braker and Mossman (*40*), ITII (*42*), and RTECS (*27*).]

Kirk-Othmer (*39*). Table 13 indicates that 5,000 ppm-v ammonia is associated with the notation: "serious edema, strangulation, asphyxia; fatal almost immediately" (*39*). The cited source of this information is Braker and Mossman (*43*).

This is a secondary source; the source quality is low. See Braker and Mossman (*43*).

Braker and Mossman (*40,43*). For summary purposes the sixth edition was obtained. Table 1 sets forth vapor concentrations, general effects, and exposure periods. Ammonia at 5,000–10,000 ppm-v is associated with "respiratory spasm, rapid asphyxia," and the exposure period indicates "rapidly fatal" (*40*). No primary source citations are provided.

This is a secondary source; the source quality is low. The exposure period is unquantified. No primary source citation is provided. This report should be rejected in favor of more completely documented reports.

ITII (*42*). A lethal inhalation concentration of 10,000 ppm-v at exposure duration 3 hr is given. No primary source citation is provided.

This is a secondary source; the source quality is low. This report should be rejected in favor of more completely documented reports.

Henderson and Haggard (*37*). This monograph is a secondary source (a review), and does not constitute a primary report of clinical or experimental findings. It includes a table titled "Physiological Responses to Various Concentrations of Ammonia." The table includes an entry indicating that ammonia is "rapidly fatal for short exposure" (*37*) at concentrations of 5,000–10,000 ppm-v. The primary source citation is apparently the previous-line citation [Ronzani (*44*)], and the phrase "short exposure" refers to 1/2 hr or 1/2–1 hr. The table also indicates that the maximum concentration allowable for short exposure (1/2–1 hr) is 300–500 ppm-v

Table 1. Inhalation effects exerted by ammonia in studies involving humans.

Concentration in air (ppm)	Exposure duration (min)	Dose times duration (ppm-v/min)	Study type	Reported effect(s)	Primary reference[a]	Secondary reference[b]
Acute exposures (within 24 hr)						
32	5	158	NOAEL	Ocular: eye irritation with lacrimation	(18)	(13)
46.8	–	–	–	Sensory: odor threshold	(12)	(13)
50	5	251	NOAEL	Ocular: eye irritation with lacrimation	(18)	(13)
72	5	359	NOAEL	Ocular: eye irritation with lacrimation	(18)	(13)
50	10	502	TC_{LO}	Respiratory: faint to moderate (5 of 6) irritation	(18)	(13)
135	5	675	TC_{LO}	Ocular: eye irritation with lacrimation	(18)	(13)
135	5	675	TC_{LO}	Respiratory: nose and throat irritation	(18)	(13)
135	5	675	TC_{LO}	Respiratory: chest irritation (1 of 6)	(18)	(13)
50	120	6,000	LOAEL	Respiratory: urge to cough; nose and throat irritation	(20)	(10)
50	120	6,000	LOAEL	Ocular: eye irritation	(20)	(10)
500	30	15,000	LOAEL	Respiratory: nasal and throat irritation; increased minute volume, cyclic pattern of hyperpnea	(19)	(10)
500	30	15,000	NOAEL	Cardiovascular: increased blood pressure and pulse rate	(19)	(10)
500	30	15,000	NOAEL	Ocular: variable lacrimation	(19)	(10)
700	–	–	–	Ocular: eye irritation, permanent injury in absence of prompt remedial measures	(34)	(13)
5,000	–	–	–	Lethality: immediate death from spasm, inflammation, or edema of the larynx	(34)	(13)
5,000	5	25,000	LC_{LO}	Lethality: specific cause of death not reported	(36)	(27)
5,000	30	150,000	Case report	Lethality: rapidly fatal	(37)	(10)
810	240	194,400	Case report	Biochemistry: some biochemical effects	(21)	(13)
7,000	180	1,260,000	LC_{LO}	Lethality: Environment Canada benchmark (draft)	(38)	(13)
5,000	–	–	Lethality	Lethality: fatal almost immediately	(39)	(43)
5,000–10,000	–	–	Lethality	Lethality: rapidly fatal	–	(43)
10,000	180	1,800,000	Lethality	Lethality: other effects not reported	(42)	(38)
30,000	5	150,000	LC_{LO}	Lethality: but value withdrawn in later editions	(27)	(38)
30,000	5	150,000	Lethality	Lethality: but reported value is erroneous (see text)	(46)	(47)
330,000 (?)	–	–	Lethality	Lethality: heart failure following lung damage	(47)	–
Apparently longer term study						
20	?	–	TC_{LO}	Olfactory: ulcerated nasal septum	(72)	(39)
20	?	–	TC_{LO}	Ocular: conjunctiva irritation	(72)	(39)
20	?	–	TC_{LO}	Respiratory: change in trachea or bronchi	(72)	(39)

Abbreviations: ?, exposure duration unquantified; LC_{LO}, lowest lethal concentration; LOAEL, lowest adverse effect level; NOAEL, no adverse effect level; TC_{LO}, lowest toxic concentration. [a]Original research or stated conclusion. [b]Source of additional information about primary source(s).

Table 2. Human exposures to airborne ammonia predicted to be lethal, based on human and animal data.

Statistic	Unit	Parameter	Haber's rule [$C^n(t)$ = constant; n = 1] 5 min	30 min	60 min	Ten Berge adjustment (n = 2) 5 min	30 min	60 min
Human lethality, based on human studies								
Number of reported lethality values (n)[a]	–	LC_{LO}	4	4	4	4	4	4
Minimum[b]	ppm	LC_{LO}	5,000	833	417	5,000	2,041	1,443
Geometric mean[c]	ppm	LC_{LO}	39,482	6,580	3,290	16,119	6,580	4,653
Arithmetic mean[d]	ppm	LC_{LO}	95,000	15,833	7,917	20,000	8,165	5,774
SD[e]	ppm	LC_{LO}	98,234	16,372	8,186	12,247	5,000	3,536
Coefficient of variation[f]	–	LC_{LO}	103	103	103	61	61	61
Human lethality, based on animal studies								
Number of reported lethality values (n)[a]	–	LC_{LO}	5	5	5	5	5	5
Minimum[b]	ppm	LC_{LO}	77,640	12,940	6,470	22,413	9,150	6,470
Geometric mean[c]	ppm	LC_{LO}	230,923	38,487	19,244	38,287	15,631	11,053
Arithmetic mean[d]	ppm	LC_{LO}	271,767	45,295	22,647	40,830	16,669	11,787
SD[e]	ppm	LC_{LO}	158,937	26,490	13,245	16,969	6,928	4,899
Coefficient of variation[f]	–	LC_{LO}	118	118	118	42	42	42
Number of reported lethality values (n)[a]	–	LC_{LO} or LC_{50}	34	34	34	34	34	34
Minimum[b]	ppm	LC_{LO} or LC_{50}	5,956	993	496	5,956	2,431	1,719
Geometric mean[c]	ppm	LC_{LO} or LC_{50}	108,478	19,369	9,946	34,455	14,559	10,433
Arithmetic mean[d]	ppm	LC_{LO} or LC_{50}	215,390	35,898	17,949	70,508	28,785	20,354
SD[e]	ppm	LC_{LO} or LC_{50}	126,400	21,067	10,533	44,827	18,300	12,940
Coefficient of variation[f]	–	LC_{LO} or LC_{50}	100	100	100	64	64	64

Abbreviations: LC_{50}, median lethal concentration; LC_{LO}, lowest lethal concentration; SD, standard deviation.
[a]Reported lethality values may appear in multiple references, and some references may report more than one of the tabulated lethality values. Thus, the number of reported lethality values differs from the number of reference citations. References are human LC_{LO}, based on human studies (34,36–39,42,43,46,47); human LC_{LO} or LC_{50}, based on animal studies: cat (29,38); mouse (26,33,38,74–79); rabbit (29,38); and rat (23,24,28,31,33,38,63,71,73,76,77). [b]Minimum: lowest among n values. [c]Geometric mean = nth root of the product of n values = sum of logarithms of n values, divided by n. [d]Arithmetic mean: sum of n values, divided by n. [e]SD = square root of the variance, where the variance = sum of n squared deviations from the arithmetic mean, divided by (n - 1). [f]Coefficient of variation = 100 × SD/arithmetic mean.

[Ronzani (*44*) and Lehmann (*45*)]; and that 2,500–4,500 ppm-v is dangerous for even short exposure (1/2 hr) (*44*).

This is a secondary source; the source quality is old but acceptable; more recent and better documented sources would be preferable. The phrase "short exposure" associated with lethality can refer to 1/2 hr or 1/2–1 hr, but seems to have been erroneously interpreted as meaning 5–10 min in derivative contemporary sources (Figure 1).

Maass (*35,36*). The German words for ammonia are Ammoniak (gas) and Salmiakgeist (solution). Maass (*35*) primarily introduced principles of biology and toxicology of chemical agents used in warfare. However, ammonia appears to be unmentioned, and its citation in the RTECS report (*27*) is erroneous. Maass (*36*) presented a table titled "Approximate Effectiveness of Gases and Vapors for Humans" [translated title] lists Ammoniak. Ammonia is listed as lethal at 5,000 ppm-v following exposure of 5–10 min duration. No primary source citation is provided for this entry. General literature is provided in an appendix on pages 249–250. However, the appendix presumably pertains to previously presented information, not to subsequent tables, some of which also have appended material. Finally, the literature cited appears to be of a general nature, including no primary research reports likely to be the original source of any toxicologic data.

These are secondary sources; the source quality is low. The lethal value—5,000 ppm-v over 10 min—lacks primary documentary support. The translated source table (*36*) title emphasizes that the tabulated values are approximate, suggesting that a definitive measurement may have been unavailable. These old reports together fail to meet current standards of technical documentation.

U.S. Coast Guard (*34*). The January 1991 edition contains a material safety data sheet for anhydrous ammonia that does not cite a lethal vapor concentration.

This is a secondary source; the source quality is low. This report should be rejected in favor of more completely documented source(s). If the 1984–1985 edition (*34*) included a lethal vapor concentration, that parameter or its value in the case of anhydrous ammonia was abandoned in the later edition. This document should be rejected.

Sax and Lewis (*46*). This document lists human 5-min inhalation LC_{LO} = 30,000 ppm-v.

This is a secondary source; the source quality is low because of erroneous information. This document should be rejected in favor of more accurate source(s). See cited reference [Mulder and Van der Zalm (*47*)].

Mulder and Van Der Zalm (*47*). A person filling a tank wagon with 25% ammonia solution failed to wear respiratory protection, and died. The report (translated from Dutch) fails to quantify the exposure duration. It is imprecise about ammonia concentrations in the breathing-zone air of the deceased, whose face had been reddened (*47*):

> Layer of lung below the superficial layer had been harmed....He had inhaled great amount of concentrated ammonia....At the moment of the mishap, the ammonia water solution spread as a thin film over the tank car. The wind direction

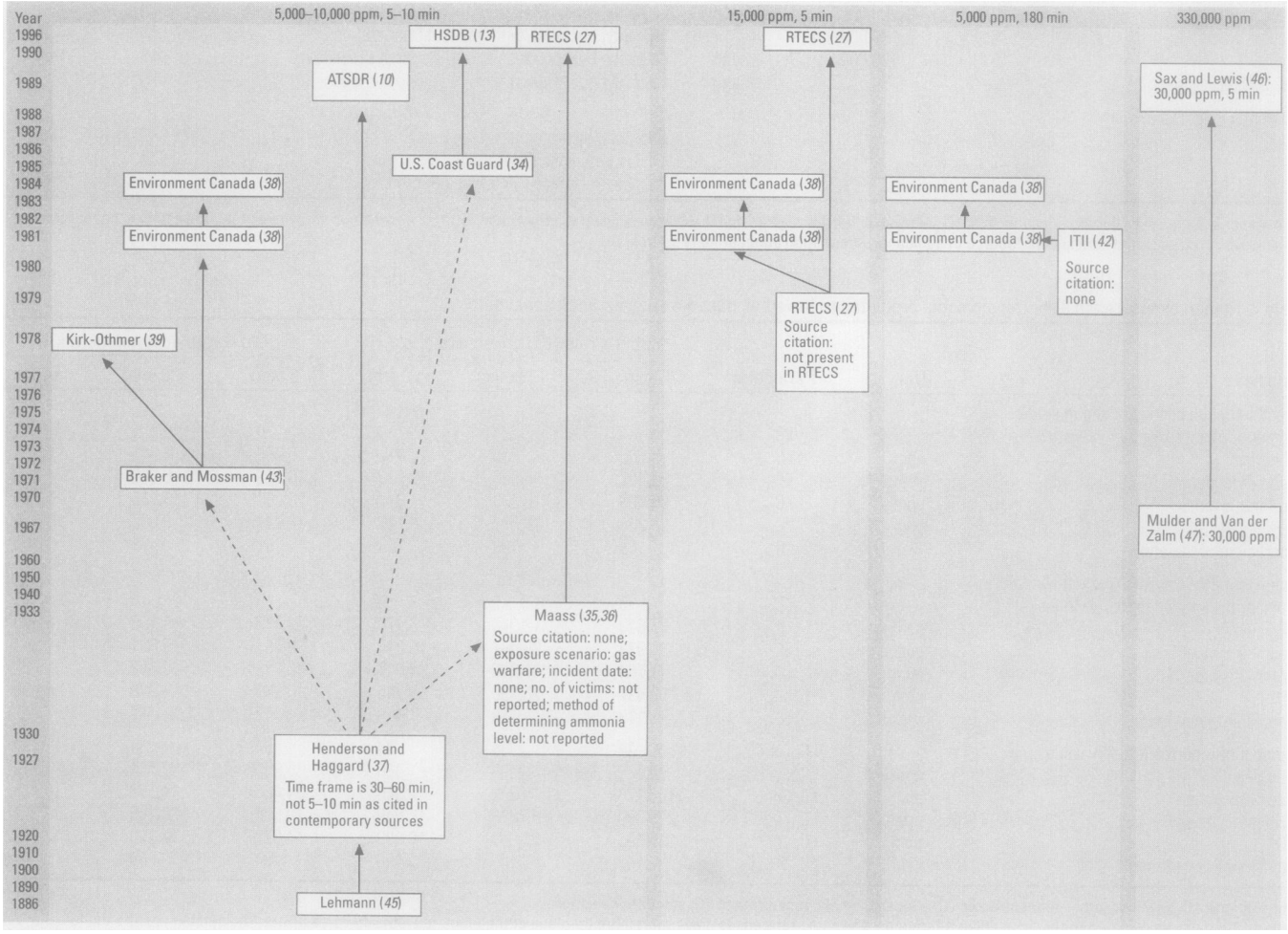

Figure 1. Evolution of four human lethality values for inhalation of ammonia. Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; HSDB, Hazardous Substances Data Bank; ITII, International Technical Information Institute; RTECS, Registry of Toxic Effects of Chemical Substances. Solid lines indicate sources that are explicitly cited. Dashed lines indicate sources that are apparent but uncited.

was toward the victim. The vapor pressure of a 25-percent (by weight) ammonia solution is 224 mm of mercury. As a consequence of that, the vapor contained 33-percent ammonia (by volume), or 330,000 ppm. Of course, under these circumstances, there was not a saturated vapor pressure at the level of the victim. The actual concentration of ammonia is unknown, but is roughly estimated to be multiple times 10,000 ppm.

The deceased had been instructed to report to the first aid room for medical attention, but instead went to the coffee room for milk. He then worked 3 hr. First aid was sought only 3 hr after the exposure incident, whereupon the patient was transferred to a clinic to have X rays performed. His heart stopped, but was restarted; he was transferred to a hospital, where his heart stopped again. The immediate cause of death, which occurred 6 hr postexposure, was heart failure, although the pathology report indicated that the underlying cause was the effect of ammonia on the deep layer of the lung, presumably creating cardiopulmonary stress that proved intolerable over the protracted period of perhaps 3–6 hr between exposure and initiation of medical attention.

This document is a primary source; the source quality is imprecise but acceptable and important. Sax and Lewis (*46*) incorrectly list a 5-min LC_{LO} of 30,000 ppm-v based on this source. The incorrect value persists in the latest edition (*48*). This accident is further evaluated below.

Accident reports. Numerous articles report lethality of anhydrous ammonia releases [e.g., (*5,6,30,47,49–59*)]. One of these cited reports (*47*) was mentioned above. However, reliable measurements of concentrations and durations of exposure are lacking. The absence of such data has motivated attempts to reconstruct ambient concentrations during accidents retrospectively, for example, based on air dispersion modeling (*6,30,52,53*) or evidence from ammonia-induced damage to biota (*30*).

Dutch accident. In the Dutch accident mentioned above (*47*), a tank was being refilled with 25% ammonia at an external temperature of 10°C over an unquantified period. Although Mulder and Van der Zalm (*47*) expressed the belief that the air at the level of the victim had not reached saturation (330,000 ppm-v), presumably the atmosphere within the tank was saturated. The ammonia-saturated vapor must have been displaced into the ambient air in close proximity to the deceased while he was on top of the tank to fill it. In addition, ammonia vapor, lighter than air at 10°C, would have been rising from the rich pool of ammonia from overflowed ammonia solution on the ground. Thus, the deceased, who "inhaled a great amount of concentrated ammonia" (*47*), appears to have been exposed, at least sporadically, to two sources of ammonia vapor at all or a reasonably high fraction of the 330,000-ppm-v saturated vapor concentration during the filling and measuring operation.

Given the time between exposure and death, Mulder and Van der Zalm (*47*) suggested that airborne ammonia concentrations equal to a reasonably large fraction of 330,000 ppm-v are not rapidly fatal. This is

Table 3. Synthesis of accident reports to discern ammonia effect levels.[a]

Category/location	Date	Estimated concentration From (ppm)	Estimated concentration To (ppm)	Geometric mean (ppm)	Release duration (min)	Exposure duration (min)	Exposed (no.)	Affected (no.)	Effect
Human fatality									
Potchefstroom, South Africa	13 Jul 73	2,500	200,000	22,361	Instant	–	–	2	Fatal
Boutte, LA	15 Dec 70	5,000	200,000	31,623	3	–	–	3	Fatal
Crete, NE	18 Feb 69	5,000	200,000	31,623	Instant	–	–	5	Fatal
Potchefstroom, South Africa	13 Jul 73	5,000	200,000	31,623	Instant	–	–	10	Fatal
Houston, TX	11 May 76	5,000	200,000	31,623	Instant	–	–	2	Fatal
Pensacola, FL	9 Nov 77	20,000	200,000	63,246	240	–	–	2	Fatal
Permanent injury									
Barnesville, MN	10 Jun 81	700	10,000	2,646	30	–	–	11	Injury: claimed permanent, to respiratory system, eyes, throat
Houston, TX	11 May 76	700	10,000	2,646	Instant	–	–	3	Injury: permanent breathing impairment
Reversible injury									
Boutte, LA	15 Dec 70	300	5,000	1,225	3	–	–	3	Injury: treated, released < 24 hr
Conway, KS	6 Dec 73	300	5,000	1,225	< 480	–	–	1	Injury: hospitalized 1 day, injuries unspecified
Conway, KS	6 Dec 73	300	5,000	1,225	< 480	–	–	1	Injury: hospitalized 6 days: eye, nose, throat, lung burns
Boutte, LA	15 Dec 70	700	10,000	2,646	3	–	–	26	Injury: hospitalized < 14 days; unspecified injuries
Pensacola, FL	9 Nov 77	20,000	200,000	63,246	240	–	–	2	Injury: children hospitalized; recovery in 1 month
Transient or clinically insignificant effects									
Houston, TX	11 May 76	300	500	387	Instant	10	–	1	NOAEL: no apparent permanent injury
Barnesville, MN	10 Jun 81	300	5,000	1,225	30	–	> 17	> 17	NOAEL: exposure without injury
Damage to flora, fauna									
Verdigris, OK	10 Jun 79	12	72	29	Instant	–	–	–	Flora: vegetative discoloration
Houston, TX	11 May 76	12	72	29	Instant	–	–	–	Flora: vegetative discoloration
[redacted], OK	7 May 76	12	72	29	240	–	–	–	Flora: wheat bleached
Crestview, FL	8 Apr 79	1,000	3,300	1,817	–	–	–	–	Flora: defoliation; other substances present, including chlorine
Houston, TX	11 May 76	2,000	2,300	2,145	Instant	–	–	–	Fauna: birds fell from trees
Blair, NE	16 Nov 70	700	10,000	2,646	150	–	–	–	Fauna: fatal to one of the two species (hogs or cattle)
Pensacola, FL	9 Nov 77	2,300	?	–	240	–	–	–	Fauna: death of small birds, wildlife
Pensacola, FL	9 Nov 77	2,300	?	–	240	–	–	–	Flora: withered trees and ground vegetation
Belle, WV	21 Jan 70	5,000	20,000	10,000	–	–	–	9	Fauna: death of nine horses

Abbreviations: ?, unknown; NOAEL, no adverse effect level.
[a]Adapted from Markham (*30*). Note that some accidents are accorded multiple listings. This is done to accommodate multiple exposure scenarios, such as might prevail at different locations in the vicinity of the accident.

in contrast to multiple sources cited and described above, and in each case found to be questionable. Given the failure of the deceased to seek immediate medical attention, and his ability to continue working, this report suggests that both the duration and the degree of the cardiopulmonary stress to which his death was attributed may have been significantly and unnecessarily exacerbated. As early as 1927, Henderson and Haggard (*37*) reported that ammonia-induced pulmonary edema, if severe, usually terminates fatally, but can be and should be treated:

> inhalation of oxygen tends to relieve the anoxemia and cyanosis and should always be begun as early as possible in the stage of gray cyanosis....By far the most important feature of treatment in such cases is absolute quiet and rest. Neglect of this requirement is common and frequently precipitates death by sudden heart failure.

Thus, the level of exposure to ammonia experienced by the deceased might be survivable for individuals comparably exposed, if they receive appropriate medical attention promptly.

Together, the facts educed from this incident suggest that a concentration of airborne ammonia to which brief exposure may be nonlethal is significantly in excess of 10,000 ppm-v, and may be as high as 330,000 ppm-v, at least for sporadic exposure. The victim must have been exposed to 330,000 ppm-v, at least sporadically, because he was located next to the fill-hole of a tank while manually pumping ammonia into it, thereby displacing a large volume of saturated ammonia vapor at 330,000 ppm-v, and he lacked respiratory protection. His face also was reddened by ammonia.

Available data do not support 330,000 ppm-v as an accurate estimate of nonlethal continuous exposure. However, inaccuracy is intrinsic when deriving knowledge from an accident reconstruction, whose success often relies on the meta-analyses of multiple accidents. In such meta-analysis, each accident reconstruction is inaccurate, but if multiple reconstructions are reasonably consistent, they may converge on a particular potency value or range of values. The consistency of multiple accidents must be evaluated based on a minimum-error exposure estimator for each accident. The arithmetic or geometric mean of the reported range of ammonia concentrations may be the mathematically best available estimator of discontinuous (on–off) exposure. A reasonable use of the mean as an exposure estimator in this case is to conservatively assume that tank filling and measuring required only 5 min, and that the equivalent continuous exposure level was equal to the mid point (arithmetic mean) of the reported range (170,000 ppm-v). A more cautious approach would be to assume that the ammonia concentration was at the geometric mean (57,446 ppm-v) rather than at the arithmetic mean of the reported concentration range.

The Bartow accident. An accident occurred on 5 December 1996 at an ammonia plant in Bartow, Florida, in which a worker drove a forklift under a storage tank of pressurized anhydrous ammonia (*60*). He severed a downwardly protruding tank nipple, releasing a strong flow of ammonia onto himself.

Table 4. Evaluation of Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations.[a]

Time from release (sec)	Modeled ammonia concentration range From (ppm)	To (ppm)	Mean	Estimated exposure duration (sec)	Cumulative exposure (sec)	Conc times duration (ppm/sec)	Equivalent mean conc (ppm) averaged over 1 min	5 min
Column →	*a*	*b*	*c*	*d*	*e*	*f*	*g*	*h*	*i*
Formula→	–	–	$(b+c)/2$	$a_5 = (a_{15} - a_0)/2$	Σe	$d \times e$	*g*/60	*g*/300
Zone 1: ≤ 50 m from release point								
0	–	–	–	–	0	–	–	–
5	641,000	641,000	641,000	7.5	7.5	4,807,500	80,125	16,025
15	365,000	365,000	365,000	12.5	20	4,562,500	76,042	15,208
30	220,000	221,000	220,500	17.5	37.5	3,858,750	64,313	12,863
50	136,000	138,000	137,000	15	52.5	2,055,000	34,250	6,850
60	109,000	113,000	111,000	15	67.5	1,665,000	27,750	5,550
80	79,600	85,000	82,300	20	87.5	1,646,000	27,433	5,487
100	62,200	68,300	65,250	20	107.5	1,305,000	21,750	4,350
120	49,800	57,300	53,550	40	147.5	2,142,000	35,700	7,140
180	28,100	37,600	32,850	60	207.5	1,971,000	32,850	6,570
240	15,800	24,100	19,950	60	267.5	1,197,000	19,950	3,990
300	7,600	13,700	10,650	60	327.5	639,000	10,650	2,130
360	1,300	7,900	4,600	60	387.5	276,000	4,600	920
420	–	2,000	2,000	60	447.5	120,000	2,000	400
480	–	–	251,093	67.5 sec (1.125 min) time-weighted average			–	–
540	–	–	58,647	447.5 sec (7.458 min) time-weighted average			–	–
600	–	–		–	–	–	–	–
660	–	–	–	–	–	–	–	–
720	–	–	–	–	–	–	–	–
Zone 2: > 50 to ≤ 100 m from release point								
0	–	–	–	–	0	–	–	–
5	–	–	–	–	0	–	–	–
15	365,000	365,000	365,000	12.5	12.5	4,562,500	76,042	15,208
30	220,000	221,000	220,500	17.5	30	3,858,750	64,313	12,863
50	136,000	138,000	137,000	15	45	2,055,000	34,250	6,850
60	109,000	113,000	111,000	15	60	1,665,000	27,750	5,550
80	79,600	85,000	82,300	20	80	1,646,000	27,433	5,487
100	62,200	68,300	65,250	20	100	1,305,000	21,750	4,350
120	49,800	57,300	53,550	40	140	2,142,000	35,700	7,140
180	28,100	37,600	32,850	60	200	1,971,000	32,850	6,570
240	15,800	24,100	19,950	60	260	1,197,000	19,950	3,990
300	8,900	13,700	11,300	60	320	678,000	11,300	2,260
360	2,900	8,300	5,600	60	380	336,000	5,600	1,120
420	–	5,500	5,500	60	440	330,000	5,500	1,100
480	–	3,200	3,200	60	500	192,000	3,200	640
540	–	1,100	1,100	60	560	66,000	1,100	220
600	–	–	202,354	60 sec (1.00 min) time-weighted average			–	–
660	–	–	39,293	560 sec (9.333 min) time-weighted average			–	–
720	–	–	–	–	–	–	–	–
Zone 3: > 100 to ≤ 200 m from release point								
0	–	–	–	–	0	–	–	–
5	–	–	–	–	0	–	–	–
15	–	–	–	–	0	–	–	–
30	–	–	–	–	0	–	–	–
50	136,000	138,000	137,000	15	15	2,055,000	34,250	6,850
60	109,000	113,000	111,000	15	30	1,665,000	27,750	5,550
80	79,600	85,000	82,300	20	50	1,646,000	27,433	5,487
100	62,200	68,300	65,250	20	70	1,305,000	21,750	4,350
120	49,800	57,300	53,550	40	110	2,142,000	35,700	7,140
180	28,100	37,600	32,850	60	170	1,971,000	32,850	6,570
240	15,800	24,100	19,950	60	230	1,197,000	19,950	3,990
300	9,100	13,700	11,400	60	290	684,000	11,400	2,280
360	5,400	8,300	6,850	60	350	411,000	6,850	1,370
420	1,900	5,600	3,750	60	410	225,000	3,750	750
480	–	4,000	4,000	60	470	240,000	4,000	800
540	–	2,400	2,400	60	530	144,000	2,400	480
600	–	–	80,118	70 sec (1.167 min) time-weighted average			–	–
660	–	–	25,821	530 sec (8.833 min) time-weighted average			–	–
720	–	–	–	–	–	–	–	–

(*Continued*)

The victim suffered cryogenic ammonia burns to his skin and eyes, as well as lung injury from inhalation of ammonia. However, he was able to extricate himself from the vehicle, run to a telephone, and summon assistance. The incident released an estimated 142 tons of ammonia over 2 hr. Although the victim was hospitalized for 19 days, he survived and eventually returned to work. Five gas dispersion models defined isolines at ground level within which ammonia levels reached ≥ 900,000 ppm-v. Assuming validity of the Ten Berge (*33*) equation with $n = 2$, this incident was reported to indicate a 5-min survivable concentration of 89,400 ppm-v.

Miscellaneous accidents. Several accidents in which ammonia concentrations were inferred by such means are evaluated in Table 3 to discern effect concentrations implied by reported ranges of exposure. Examination of Table 3 reveals an absence of reliable exposure duration data. Nonetheless, the geometric mean of reported lethal exposure ranges is approximately 30,000 ppm. A reasonably conservative exposure would appear to be 5 min based on the amount of time required for dissipation of ammonia, as inferred from the ammonia release accident in Potchefstroom. This accident is evaluated in Tables 4–6 and in supporting text.

The Potchefstroom accident. On 13 July 1973 an ammonia bullet tank in Potchefstroom failed, releasing 38 metric tons of anhydrous ammonia. The basis for exposure concentrations in Table 3 was the World Bank Hazard Analysis (WHAZAN; Technica, London) air dispersion model. Higher concentrations in Table 4 were based on the more modern HGSYSTEM model (Shell Research, Ltd., London) (*53*), which better accounts for the initially heavier-than-air density of cryogenic (adiabatically cooled) ammonia. WHAZAN modeling assumptions used by Pederson and Selig (*6*) in reconstructing the Potchefstroom accident were applied as inputs to HGSYSTEM (*53*). Cold, relatively high-density ammonia remains within the breathing zone before equilibrating with ambient outdoor temperature. Consequently, with HGSYSTEM, fatality rates in accident zones correlate with higher ammonia concentrations, and with lower acute toxic potency, of inhaled ammonia.

As Table 4 indicates, the exposure duration in zone 1 was estimated at 448 sec (7.5 min). The time-weighted average exposure over that duration was 58,647 ppm-v (Table 4), with 60% mortality (Table 6). Values for other zones are as follows: zone 2, 9.3 min, 39,293 ppm-v, and 26% mortality; zone 3, 8.8 min, 25,821 ppm-v, and 83% mortality (this value must be considered unreliable because other exposed individuals are presumed to have left the scene uncounted); and zone 4, 9.3 min, 18,073 ppm-v, and 0% mortality (Tables 4 and 6).

A spectrum of predicted ammonia concentration-effect benchmarks is calculated in Table 4 based on observed values, which are also tabulated. Most notably, peak, 1-min, and 5-min human inhalation LC_{50} and LC_0 values are tabulated. These LC_{50} values are 560,000 ppm-v (peak), 268,832 ppm-v (1 min), and 83,322 ppm-v (5 min); LC_0 values are 82,300 ppm-v (peak), 84,883 ppm-v (1 min), and 33,737 ppm-v (5 min).

Personal communications. To augment the available database pertaining to ammonia lethality concentrations, a series of telephone inquiries was implemented. Target contacts included representatives of insurance companies that might have experienced losses associated with anhydrous ammonia release, chemical companies manufacturing ammonia, trade associations representing industries facing challenges of handling ammonia, and federal agencies regulating ammonia manufacture, transport, and/or use. No data were found, and no individual indicated that additional human lethality data could be found.

Table 4. *Continued.*

Time from release (sec)	Modeled ammonia concentration range From (ppm)	To (ppm)	Mean	Estimated exposure duration (sec)	Cumulative exposure (sec)	Conc times duration (ppm/sec)	Equivalent mean conc (ppm) averaged over 1 min	5 min
Column → *a*	*b*	*c*	*d*	*e*	*f*	*g*	*h*	*i*
Formula→	–	–	$(b + c)/2$	$a_5 = (a_{15} - a_0)/2$	Σe	$d \times e$	$g/60$	$g/300$
Zone 4: 250 m from release point								
0	–	–	–	–	0	–	–	–
5	–	–	–	–	0	–	–	–
15	–	–	–	–	0	–	–	–
30	–	–	–	–	0	–	–	–
50	–	–	–	–	0	–	–	–
60	–	–	–	–	0	–	–	–
80	79,600	85,000	82,300	20	20	1,646,000	27,433	5,487
100	62,200	68,300	65,250	20	40	1,305,000	21,750	4,350
120	49,800	57,300	53,550	40	80	2,142,000	35,700	7,140
180	28,100	37,600	32,850	60	140	1,971,000	32,850	6,570
240	15,800	24,100	19,950	60	200	1,197,000	19,950	3,990
300	9,100	13,700	11,400	60	260	684,000	11,400	2,280
360	5,800	8,300	7,050	60	320	423,000	7,050	1,410
420	2,800	5,600	4,200	60	380	252,000	4,200	840
480	–	4,050	4,050	60	440	243,000	4,050	810
540	–	2,800	2,800	60	500	168,000	2,800	560
600	–	1,500	1,500	60	560	90,000	1,500	300
660	–	–	63,663	80 sec (1.333 min) time-weighted average			–	–
720	–	–	18,073	560 sec (9.333 min) time-weighted average			–	–

Conc, concentration.
[a]Based on data reported by Mudan and Mitchell (*53*).

Discussion and Conclusions

Odor Threshold and Vapor Density

The reported range of the ammonia odor threshold (0.04–57 ppm-v) corresponds to the range of occupational standards and guidelines for prolonged exposure to ammonia. The odor threshold is also significantly below the ammonia immediately dangerous to life and health (IDLH) value [a National Institute for Occupational Safety and Health (NIOSH) parameter] of 300 ppm-v. This value represents the concentration which, if exceeded for 30 min, may render an exposed individual incapable of escape. Consequently, the distinct odor of ammonia and its relatively low odor threshold constitute excellent warning properties. Individuals would be capable of detecting ammonia nearly simultaneously with the onset of exposure. In circumstances in which ammonia might gradually increase to clinically significant concentrations, the low odor threshold may constitute an early warning system, alerting exposed individuals of the need to take corrective and/or protective actions. The low odor threshold of ammonia may be regarded as a risk-mitigating factor rather than a risk-enhancing factor, as compared with more-difficult-to-detect gases such as carbon monoxide. Nonetheless, the excellent warning properties of ammonia do not constitute a substitute for its routine quantitative monitoring at potential release sites.

The finding that gaseous ammonia exhibits a density of 0.6 relative to air indicates that ammonia releases would tend to rise in tranquil air. However, liquid ammonia may be cryogenically cooled. Its initial density upon release may be heavier than air (*53*). Equilibration with outdoor ambient temperature would be expected to result in a gradual transition to a lighter-than-air condition.

Nonetheless, indoor settings may inhibit effective ammonia dissipation, and both

outdoor and indoor air might be sufficiently turbulent to overcome the density-driven tendency of ammonia to rise out of the personal breathing zone of occupationally exposed individuals. In contrast, environmentally exposed individuals presumably would be situated outdoors, where ammonia typically would not be confined. The low vapor density of ammonia relative to air may therefore be regarded as a risk-mitigating factor rather than a risk-enhancing factor as compared to a heavier-than-air gas such as chlorine.

Relationship between Concentration and Exposure Duration in Producing Toxic Effect

An approximation in toxicology (sometimes termed Haber's rule) is that the product of the dose and duration of exposure to a particular toxic substance equals a constant value (*6,33*) according to the equation: $C^n(t)$ = constant, where C is the concentration, t is the exposure duration, and n is unity (= 1).

This rule is approximate for several reasons (*33*), the explication of which is beyond the scope of this report. However, the rule often may be usefully applied to closely spaced exposure durations such as 5 min versus 1 hr. Thus, a 5-min inhalation exposure to a particular concentration in air might be approximately equivalent to a 1-hr exposure to 1/12th of the 5-min concentration. Alternatively, Ten Berge et al. (*33*) empirically determined that n = 2 for mice and rats, and suggest that n might = 2 for humans as well. The relationship elucidated above, with the value of n chosen from 1 to 2, may be used to adjust ammonia concentrations over varying exposure durations to the equivalent concentration corresponding to any chosen exposure duration from 5 min to 1 hr (*6*). This report uses both extremes—n = 1 and n = 2.

Table 5. Evaluation of the Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations: summary of fatality rates.[a]

Fatality rate (%)	Ammonia level: Peak	1 min (ppm)	5 min[b]
Observed			
0	0	0	0
0	82,300	84,883	33,737
26	365,000	236,080	73,347
60	641,000	282,479	87,479
Calculated[c]			
0	82,300	84,883	33,737
10	191,341	143,036	48,972
20	300,383	201,188	64,207
30	398,000	241,539	75,010
40	479,000	255,185	79,166
50	560,000	268,832	83,322
60	641,000	282,479	87,479
70	722,000	296,126	91,635
80	803,000	309,773	95,791
90	884,000	323,420	99,947
100	965,000	337,067	104,103

[a]Based on data reported in Mudan and Mitchell (*53*). [b]Adjusted from 7 or 9 min. [c]Interpolating or extrapolating observed values.

Adoption of Acceptable Risk Criteria

Risk acceptability is a subjective judgment, and cannot be defined scientifically. However, qualitatively different adverse health effects may be proposed as being acceptable, and selection of an acceptable risk may be made from any of a variety of adverse effects. These effects might range from no adverse health effect, to clinically insignificant effects, to reversible injury, to permanent injury, or to lethality. Ammonia benchmarks may be quantified based on holistic consideration of toxicologic data, including human clinical data, animal bioassay data, and reports of industrial ammonia release accidents. Selected acute toxicology benchmarks for ammonia are summarized in Table 7. Ideally, all data sources converge on a single value for each toxicologic benchmark parameter to be quantified. However, Table 7 reveals significant disparity. One source of such disparity is revealed in "Results"; that is, a fundamental conflict between contemporary accident reconstruction results versus largely anecdotal data derived from reports of ammonia potency dating back, in some cases, to the years when ammonia competed with mustard gas, chlorine, and other war gases whose primary purpose was to kill enemy soldiers engaged in trench warfare. Potency values reported for lethality in that context have persisted in the contemporary literature, as depicted in Figure 1. Multiple industrial accident reconstructions point to a lower potency of ammonia than suggested by apparently anecdotal data, and the lower potency suggested by the accident reconstruction data is consistent with animal bioassays using multiple species.

Fatal Exposure Concentration

The National Research Council Committee on Toxicology defines three levels of community emergency exposure levels (CEELs, since renamed AEGLs). AEGL-3 is defined to protect members of the general population, including susceptible but excluding hypersusceptible individuals, against "death or life-threatening effects...for example, pulmonary edema, cardiac failure, or cancer" (*1*). The benchmark for fatal exposure to ammonia may be derived from American Industrial Hygiene Association (AIHA) emergency response planning guidelines (ERPGs), animal bioassay data, human data, and reports of fatal accidents. These sources should produce consistent results but, in the case of ammonia, they do not. They will be synthesized to produce a conservative but realistic estimate of the ammonia lethality concentration for short exposure durations.

Table 6. Evaluation of the Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations: summary by zone.[a]

	Zone 1	2	3	4
Individuals exposed (no.)	10	27	6	?
Fatalities (no.)	6	7	5	0
Survivors (no.)	4	20	1	All
Fatality rate	0.60	0.26	0.83	0.00
Survival rate	0.40	0.74	0.17	1.00

?, unknown.
[a]Based on data reported in Mudan and Mitchell (*53*).

AIHA ERPG-3. The AIHA (*61*) defines ERPG-3 as

> [t]he maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.

The ERPG-3 value for ammonia is 1,000 ppm-v. According to the AIHA,

> [t]his level may cause severe eye and nasal irritation [*19,20,62*]; however, based on animal toxicology data [*63,64*] lethality would not be expected.

The 1-hr 1,000-ppm-v ERPG-3 is equivalent to a 5-min value of 12,000 ppm-v using Haber's rule or 3,464 ppm-v using Ten Berge's adjustment with n = 2. As indicated in "Results" and in Table 2, higher values are also sublethal. Indeed, the AIHA's ERPG-3 value is not based on lethality and therefore already incorporates an unquantified safety factor. The actual ammonia lethality level cannot be reconstructed based on the AIHA's documentation, and the ERPG-3 must be rejected as downwardly adjusted and irrelevant.

Table 7. Ammonia acute inhalation toxicology benchmarks.

Benchmark	Conc (ppm-v)	Duration (min)
Odor threshold	0.04–57	> 0
Standards and guidelines[a]		
ACGIH STEL	35	15
AIHA ERPG-2 (injury/escape)	200	60
NIOSH IDLH	300	30
AIHA ERPG-3 (lethality)	1,000	60
Clinically insignificant effects	50	10
Irreversible effects	7,051	5
	2,879	30
	2,035	60
Fatal exposure	> 33,737	5
	> 5,623	30

Abbreviations: ACGIH, American Conference of Governmental Industrial Hygienists; AIHA, American Industrial Hygiene Association; Conc, concentration; ERPGs, Emergency Response Planning Guidelines; IDLH, immediately dangerous to life or health; NIOSH, National Institute for Occupational Safety and Health; STEL, short-term exposure limit.
[a]National Library of Medicine (*13*).

Animal studies. Numerous animal bioassay reports were addressed in "Results" (Table 2). They were adjusted to equivalent HECs using parameters for dose conversion among species (*7,8*) and EPA methodology (*8*). Although the LC_{LO} parameter is more conservative than the LC_{50} parameter, the dearth of LC_{LO} values resulted in LC_{50} values that are lower than the LC_{LO} values (Table 2). Consequently, both parameters will be considered together.

Concentrations of airborne ammonia whose lethality to humans is estimated based on animal bioassay studies produced an arithmetic mean inhalation LC_{LO} or LC_{50} value of 215,390 ppm-v at 5 min; 35,898 ppm-v at 30 min; and 17,949 ppm-v at 60 min in accordance with Haber's rule, or 70,508; 28,785; and 20,354 ppm-v, respectively, using Ten Berge's adjustment with n = 2. Geometric mean values were 108,478; 19,369; and 9,946 ppm-v according to Haber's rule, and 34,455; 14,559; and 10,433 ppm-v using Ten Berge's adjustment. The minimum human equivalent LC_{LO} or LC_{50} value was reported from guinea pig data: 5,956 ppm-v at 5 min; 993 ppm-v at 30 min; and 496 ppm-v at 60 min according to Haber's rule, and 5,956; 2,431; and 1,719 ppm-v using Ten Berge's adjustment. These minimum values are outliers, however, and are contradicted by other data on guinea pigs (*38*): 35,957 ppm-v at 5 min; 14,679 at 30 min; 10,380 ppm-v at 60 min using Haber's rule, and 8,040; 4,020; and 1,005 ppm-v using Ten Berge's adjustment with n = 2.

The upper respiratory systems of mammals, including humans, may scrub ammonia, especially during nose breathing. This process affords some protection of the lower respiratory system from injury. This protection, however, tends to be lost quickly at high ammonia concentrations, which saturate the scrubbing capacity of upper respiratory structures. Some lethality values derived from animal bioassays (of rabbits, for example) involved cannulation, and are highly conservative. These values are conservative because cannulation, usually at the windpipe, bypasses the upper respiratory tract, reducing the concentration of ammonia necessary to cause toxic injury to the lower respiratory tract. Animal studies involving cannulation, therefore, tend to reduce ammonia effect levels such as lethality. In contrast, humans exposed to ammonia in accidental releases are unlikely to have been cannulated, and may scrub ammonia by reverting to nose breathing, or even by breathing with mouths covered with wet cloth.

Human data, apparently anecdotal. Human lethality values derived from animal data were significantly higher than lethality values derived from apparently anecdotal reports of lethality following human exposure. The latter produced an arithmetic mean inhalation lethality value of 95,000 ppm-v at 5 min; 15,833 ppm-v at 30 min; and 7,917 ppm-v at 60 min in accordance with Haber's rule; or 20,000; 8,165; and 5,774 ppm-v, respectively, using Ten Berge's adjustment with n = 2. Geometric mean values were 39,482; 6,580; and 3,290 ppm-v according to Haber's rule, and 16,119; 6,580; and 4,653 ppm-v using Ten Berge's adjustment. Thus, a disparity exists between lethality data derived from animal versus human studies, and this disparity is approximately 3-fold when arithmetic mean lethality values are considered (215,390 ppm-v/95,000 ppm-v = 2.3 at 5 min using Haber's rule; 70,508 ppm-v/20,000 ppm-v = 3.5 (also at 5) min using Ten Berge's adjustment).

Accident reports. The toxicologic findings discussed above and presented in Table 2 are quantitatively complex but qualitatively simple: predictions of ammonia concentrations that would be lethal to humans tend to be significantly lower than lethal concentrations inferred from animal studies. This is true under Haber's rule [$C^n(t)$ = constant, with n = 1] or Ten Berge's adjustment with n = 2 (based on data on mice and rats).

Considered alone, the human data are questionable, as explained previously. Considered in the context of the animal data, the human data are further questionable: no obvious basis is evident for the apparently greater sensitivity of humans than animals. This disparity between human lethality values inferred from human data versus animal data motivated reconstruction of the 1973 industrial accident in Potchefstroom, which killed 18 people, as described and tabulated in Tables 4–6 and depicted in Figure 2.

Figure 2 illustrates the effect of increasing peak, 1 min, and 5-min time-weighted average anhydrous ammonia concentrations in air on the human fatality rate. The LC_{50} values are estimated to be a peak of 560,000 ppm-v, a 1-min mean of 268,832 ppm-v, and a 5-min mean of 83,322 ppm-v. Longer term values were not generated because the air modeling addressed an exposure period of under 10 min.

The Potchefstroom accident reconstruction indicates ammonia lethality levels significantly higher than both the human data and animal bioassay data. However, the accident reconstruction is complicated because the plant contained a control room and other structures that were at least partially enclosed. These potential refuges would tend to elevate the apparent resistance of individuals to ammonia. A conservative interpretation of the accident reconstruction, therefore, is appropriate. For example, the 5-min concentration producing 0% mortality (LC_0) determined from zone 4, where no fatalities occurred, was 33,737 ppm-v (Table 6). This value is consistent with human lethality levels derived from the animal bioassay data, but is still higher than lethality levels inferred from the human data. It is also consistent with the Mulder and Van der Zalm report (*47*), in which an individual died, possibly unnecessarily, following exposure to a sizable but unknown fraction of 330,000-ppm-v saturated ammonia vapor. A reasonable inference from analysis of available accident data is that they validate adjustment of animal lethality concentrations to human equivalent values.

Irreversible Injury Concentration

AEGL-2 is defined by the National Research Council Committee on Toxicology to protect members of the general population, including susceptible but excluding hypersusceptible individuals, against permanent or long-lasting effects, impairment of the ability to escape, or disablement; for example, as a result of "severe eye or respiratory irritation, disorientation, and organ damage" (*1*). The IDLH and the ERPG-2 parameters are candidates for the irreversible injury (AEGL-2) benchmark, but the values assigned these parameters in the case of ammonia are flawed. However, the IDLH or the ERPG-2 methodology might be adopted, rather than the IDLH or ERPG-2 value for ammonia. Appropriate use of these parameters is addressed below.

AIHA ERPG-2. A reasonable candidate value for the benchmark for irreversible injury is 200 ppm-v, which corresponds to the AIHA ERPG-2 value (*65*). The AIHA (*65*) defines ERPG-2 as

> [t]he maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.

The ERPG-2 for ammonia is 200 ppm-v. According to the AIHA (*65*),

> [t]here is likely to be strong odor and some eye irritation at this level [*20,66,67*], but serious health effects are unlikely. Rats continuously exposed to 180 ppm for 90 days showed no adverse effects [*64*], and humans repeatedly exposed to 100 ppm for six weeks developed only slight eye irritation [*66*].

The ERPG-2 value does not represent an irreversible injury level, but an eye irritation level—and not the highest tolerable. Silverman et al. (*19*) reported that all seven individuals voluntarily exposed to ammonia at 500 ppm-v for 30 min tolerated the exposure without adverse effect or inability to escape. A fundamental problem with ERPG-2 is that eye irritation and associated lacrimation occur over a wide range of concentrations,

with effects varying from annoyance to clinical significance. Impairment of vision may reduce escape ability, but escape ability is reduced routinely by factors such as darkness during industrial emergencies, either because they may occur at night or because power may be lost during daytime emergencies in structures not illuminated internally by sunlight.

NIOSH IDLH. Another reasonable candidate value for the benchmark for irreversible injury is 300 ppm-v for 30 min, which corresponds to the NIOSH IDLH value (*68*) (Table 7). Preference of this regulatory criterion over toxicologic data would seem desirable, given the apparent unavailability of detailed dose–response human toxicology data documenting irreversible injury from ammonia inhalation. However, use of the IDLH value is undesirable. The IDLH value is based on secondary literature (*68*), and NIOSH indicated that the primary literature was not examined. NIOSH investigators indicate that

> [t]he chosen IDLH is based on the statement by AIHA (1971) that 300 to 500 ppm for 30 to 60 minutes have been reported as a maximum short exposure tolerance (Henderson and Haggard 1943).

However, AIHA (*65*) is superseded by AIHA (*61*), which states that 300–500 ppm-v is a maximum 1-hr exposure, irritating the eyes, nose, and throat. The AIHA (*61*) does not state that 300–500 ppm-v is the maximum tolerable, nor that the time frame over which its effects might become intolerable is 30 min. The AIHA also does not state that 300–500 ppm-v might render an exposed individual incapable of escape within 30 min. Indeed, the AIHA (*61*) further states that 1,000 ppm-v represents

> [t]he maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects....This level may cause severe eye and nasal irritation; however, based on animal toxicology data lethality would not be expected.

In supporting an IDLH value of 300 ppm-v, NIOSH (*68*) indicates that "AIHA (1971) also reports that 5,000 to 10,000 ppm are reported to be fatal (Mulder and Van der Zalm 1967)." However, Mulder and Van der Zalm (*47*) do not say this. Indeed, they cite the 5,000- to-10,000-ppm-v lethality range, but primarily for the purpose of refuting it. They indicate that the deceased was exposed to many times 10,000 ppm-v, that he ignored instructions to report to the infirmary for timely medical attention, and that he was able to resume work for 3 hr despite his injuries.

NIOSH (*68*) also states that "exposures for 30 min to 2,500 to 6,000 ppm are considered dangerous to life (Smyth 1956) [*69*]." However, Smyth (*69*) is a secondary source that compiled suggested "hygienic standards for *daily* inhalation" (emphasis added).

The NIOSH report fails to indicate how the lethality values it cites might be related to its selection of an IDLH. However, one might surmise that NIOSH regards these lethality values as LC_{50} values, which might be equated to 10 times a preliminary IDLH value (*70*):

> ...LC values (after 'adjusting' if necessary to 30 min) were divided by a safety factor of 10 to determine a 'preliminary' IDLH for comparison purposes.

Thus, the presumed lethality values of 5,000–10,000 ppm-v would support IDLH values of 500–1,000 ppm-v, and 2,500–6,000 ppm-v would support an IDLH of 250–600 ppm-v. However, the lethality values cited by NIOSH appear to be unreliable based on analyses presented herein.

Potchefstroom accident reconstruction. The irreversible injury concentration may be derived in a manner consistent with derivation of the IDLH value. The IDLH is initially estimated as one-tenth the (animal) LC_{50} value. Subsequent adjustment may be necessary based on examination of other types of data, such as explosivity limits and the concentrations at which respiration is reduced 50% in mice or rats exposed for 10 min. The mean 5-min LC_{50} value derived earlier from animal bioassay data is 70,508 ppm-v using the Ten Berge adjustment, which in this case is more conservative than the Haber's rule value (215,390 ppm-v). The 5-min LC_{50} value derived earlier from the Potchefstroom accident reconstruction is 83,322 ppm-v, but this may represent an upper limit, as discussed previously. Using the mean 5 min LC_{50} value from animal bioassays produces an irreversible injury concentration of 7,051 ppm-v at 5 min; 1,175 ppm-v at 30 min; and 588 ppm-v at 1 hr using Haber's rule; and 7,051; 2,879; and 2,035 ppm-v, respectively, using Ten Berge's adjustment with $n = 2$. These values are approximately one-fifth the 5-min lethality value of 33,737 ppm-v.

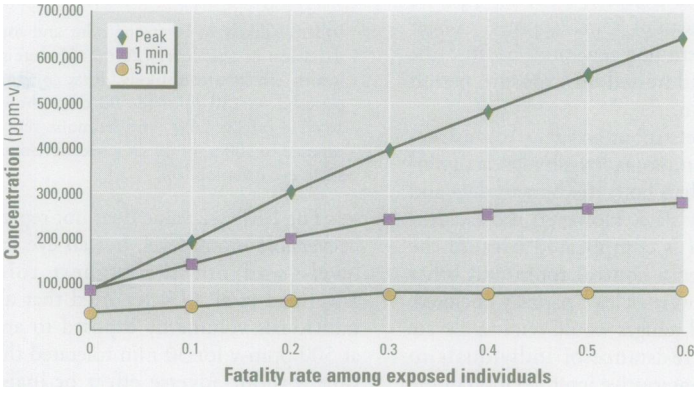

Figure 2. Estimated peak, 1-min, and 5-min lethal ammonia concentrations based on fatalities In a 1973 Potchefstroom, South Africa, accident. LC_{50}, median lethal concentration. Peak LC_{50}, 560,000 ppm; 1-min LC_{50}, 268,832 ppm; 5-min LC_{50}, 83,322 ppm. Based on data reported in Mudan and Mitchell (*53*).

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